UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

SERONO, INC.,	)	
	)	
Plaintiff,	)	
	)	
vs.	)	**Civil Action No. 02-11832 MLW**
	)	
FERRING PHARMACEUTICALS, INC.,	)	
	)	
Defendant.	)	
	)	

FERRING PHARMACEUTICALS, INC.'S OPENING BRIEF ON CLAIM CONSTRUCTION

Pursuant to the Court's Scheduling Order, Defendant Ferring Pharmaceuticals, Inc. ("Ferring") hereby submits its Opening Brief on Claim Construction.

I. INTRODUCTION

On September 18, 2002, Serono filed a Complaint with this Court alleging that, in selling its gonadotropin drug Bravelle™, Ferring induces its customers' infringement of two Serono patents. Serono's patents are U.S. Patent Nos. 4,845,077 (the "'077" patent) and 4,589,402 (the "'402" patent). The '077 patent dates to an application filed on April 3, 1984, and the '402 patent dates to an application filed on July 26, 1984. Neither patent contains product claims. They are both method patents.

Ferring competes with Serono in the market of gonadotropin treatment of female infertility. As part of that competition, Ferring sells Bravelle™, a highly-purified mixture of two hormones made in the human pituitary: follicle stimulating hormone (FSH) and luteinizing hormone (LH).

Of the two patents in suit, at least six claims – and perhaps up to nine claims – are at issue in this case. Certainly '077 patent claims 1, 2, 8, and 9 and '402 patent claims 1 and 3 are at issue. Additionally, Serono has recently attempted to add three additional claims to those at issue: '077 patent claims 13, 14, and 16.[1]

Among these nine claims are found five claim terms requiring construction relating primarily to the claimed methods of using FSH. The parties do not agree as to what Serono's inventors meant when, in claims 1, 2, 8, 9 of the '077 patent and claims 1, 3 of the '402 patent, they claimed methods of using "FSH in the absence of exogenous LH," or "FSH alone . . . without the presence of exogenous LH." Also among the nine claims are three claim terms requiring construction relating primarily to methods of suppressing estrogen variability with drugs called gonadotropin releasing hormone antagonists. The parties may not agree on what the inventors meant in claims 13, 14 and 16 of the '077 patent when they claimed a "method of suppressing estrogen variability" in infertile women.

Before discussing these claim terms more specifically, Ferring will provide the Court with some general background regarding the technology and physiology relating to the patented subject matter.

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[1] The Court set dates for the briefing of claim construction issues in August, 2003. On the eve of the Court's date for the parties' service of claim construction charts, Serono served by facsimile an unverified supplemental response to Ferring's interrogatories purporting to put three additional claims in issue: claims 13, 14, and 16 of the '077 patent. Ferring objects to Serono's untimely supplemental response. Without waiving its objection, Ferring addresses these additional claims here. Two weeks after the claim construction charts were due for service and one day before this brief was due for filing, Serono served an untimely "amended" claim chart changing its proposed interpretations of claims 1, 2, 8, and 9 of the '077 patent and claims 1 and 3 of the '402 patent. Due to the untimely nature of these latest submissions, Ferring objects to the filing and does not address the amended claim constructions herein, but reserves the right to discuss these issues, should the Court find that these tardy filings need to be addressed.

II. BACKGROUND OF THE PATENTED SUBJECT MATTER

The claim terms requiring construction all relate to Serono's patented methods of using hormone drug treatments to treat infertile women. These drug treatments affect women's ovaries, their pituitary hormones, and their sex hormone estrogen.

The human female ovary contains ova – unfertilized eggs – within follicles. The follicles are sensitive to two hormones made in the pituitary glands that act on the ovaries: FSH and LH. Because these hormones affect the ovary, a sex organ, they are termed "gonadotropins." A woman's own pituitary-made gonadotropins are termed "endogenous" gonadotropins. Gonadotropins prepare ovarian follicles to mature and rupture. The gonadotropin FSH stimulates ovarian follicular development. FSH also stimulates production of an important female sex hormone – estrogen – by the ovary. During the normal female menstrual cycle, following a mid-cycle surge of pitutary LH, a single follicle on one ovary ruptures to release an ovum (the process of "ovulation") which then passes down the fallopian tubes, into the uterus, to await fertilization by sperm. *See* '077 Patent, col. 1, ll. 16-19 and 41-50 attached as Exhibit A to the Declaration of M. Reed Staheli (Staheli Decl., Ex. A).

Not all gonadotropins are endogenous, of course. Gonadotropins may be administered as drugs. When so administered, they are termed "exogenous" gonadotropins. Bravelle™ is just such a drug – a mixture of the two exogenous gonadotropins FSH and LH. The FSH and LH in Bravelle™ are extracted from the hormone-rich urine of post-menopausal women. Bravelle™ contains up to 2% LH along with the FSH. Ferring has FDA approval to label and market Bravelle™ for use in treating female infertility. While Ferring has FDA approval to label Bravelle™ for use in treating female infertility, the FDA has not approved Bravelle™ for any other use, and Ferring does not promote Bravelle™ for "off-label" uses.

Exogenous gonadotropins like Bravelle™ may be given to infertile women to induce fertilization in a process termed *in vivo* fertilization (also known as "ovulation induction" or "OI"). In that process, it is not uncommon for physicians to administer another exogenous gonadotropin "human chorionic gonadotropin" ("hCG") which causes ovulation. Exogenous gonadotropins like Bravelle™ may also be given to induce follicular maturation and rupture such that ova may be removed from a woman's body, fertilized with sperm in the laboratory, and then implanted in the uterus in a process termed *in vitro* fertilization or "IVF". *See* '077 Patent, col. 1, ll. 58-62, col. 2, ll. 58-63; '402 Patent, col. 1, ll. 55-59, col. 2, ll. 60-64 (Staheli Decl., Exs. A and B). Methods of using exogenous gonadotropins to treat infertility by OI and IVF are among the claims in issue: '077 patent claims 1, 2, 8, and 9; and '402 patent claims 1 and 3. (*See* Staheli Decl., Exs. A and B).

Gondadotropins like FSH and LH are themselves subject to hormonal control. The pituitary gland normally releases (secretes) additional amounts of FSH and LH when a hormone made at the base of the brain called "gonadotropin releasing hormone" (abbreviated "GnRH") binds to pituitary receptor sites. *See, e.g.,* '077 Patent, col. 2, ll. 2-5 (Staheli Decl., Ex. A). Synthetic – laboratory-made – compounds known as "gonadotropin releasing hormone agonists" ("GnRH-agonists") mimic GnRH. These GnRH-agonists bind to receptor sites and stimulate strong pituitary secretion of FSH and LH, such that there is a rise in FSH and LH followed by a fall due to exhaustion. A very different class of synthetic compounds are known as "gonadotropin releasing hormone antagonists" ("GnRH-antagonists") which interfere with the action of GnRH on the pituitary by binding to and blocking the pituitary receptor sites. GnRH-antagonists also "eliminate endogenous pituitary FSH and LH secretion." '077 Patent, col. 4, ll. 21-42 (Staheli Decl., Ex. A).

In the '077 patent claims 13, 14 and 16, Serono has patented methods of using such GnRH-antagonists – but not GnRH-agonists – in a "method of suppressing estrogen variability in response to gonadotropin treatment." While Bravelle™ has been approved for use as a gonadotropin, it has never been approved for use as a releasing hormone antagonist, or to eliminate or reduce endogenous gonadotropin production, or to suppress estrogen variability. Ferring has never labeled or promoted Bravelle™ as a gonadotropin antagonist, or as a way to eliminate or reduce endogenous FSH and LH, or as a way to suppress estrogen variability.

III. LEGAL STANDARDS FOR CLAIM CONSTRUCTION

The Court is required to determine what the language of the claims means. *Markman v. Westview Instruments, Inc.*, 52 F.3d 967, 979 (Fed. Cir. 1995), *aff'd*, 517 U.S. 370 (1996). Specifically, the role of a Court in patent claim construction is to determine what the language of the claims would mean to a person of ordinary skill in the art. *Id.* at 986 ("the focus is on the objective test of what one of ordinary skill in the art at the time of the invention would understand the term."). To do this, the Court must determine what the disputed claim terms mean by following accepted legal principles of claim construction and evaluating the evidence in light of those principles.

Claim construction begins with examining the intrinsic evidence, *i.e.*, the claims, the other portions of the specification, and the prosecution history. *Gart v. Logitech, Inc.*, 254 F.3d 1334, 1339 (Fed. Cir. 2001) *cert. denied*, 534 U.S. 1114 (2002); *Biogen, Inc. v. Berlex Labs., Inc.*, 113 F. Supp. 2d 77, 96 (D. Mass. 2000) ("[T]he context of the words in claims is critical to understanding their meaning," the context gives "a full understanding of what the inventors actually invented and intended to envelop with the claim," and "[t]he specification and prosecution history illuminate what was invented and intended to be covered by a claim."),

citing *Renishaw PLC v. Marposs Societa' per Azioni*, 158 F.3d 1243, 1250 (Fed. Cir. 1998) and *Comark Communications, Inc. v. Harris Corp.*, 156 F.3d 1182, 1187 (Fed. Cir. 1998).

"[T]he analytical focus must begin and remain centered on the language of the claims themselves, for it is that language that the patentee chose to use to particularly point out and distinctly claim the subject matter which the patentee regards as his invention." *Texas Digital Sys., Inc. v. Telegenix, Inc.*, 308 F.3d 1193, 1201-02 (Fed. Cir. 2002) *cert denied*, 123 S. Ct. 2230 (2003) (internal quotations omitted). There is a "heavy presumption" that claim terms carry their ordinary meaning. *Johnson Worldwide Assocs., Inc. v. Zebco Corp.*, 175 F.3d 985, 989 (Fed. Cir. 1999) (directional limitations rejected and ordinary and accustomed meaning of "heading signal" controlled).

Importantly, where a claim "does not appear to convey any special technical meanings" its terms will be given their plain and ordinary English meaning. *Middleton, Inc. v. Minnesota Mining & Mfg. Co.*, 311 F.3d 1384, 1387 (Fed. Cir. 2002). Dictionary definitions may be consulted in establishing a claim term's ordinary meaning as long as the intrinsic record is consulted "to identify which of the different possible dictionary meanings of the claim terms in issue is most consistent with the use of the words by the inventor." *Texas Digital*, 308 F.3d at 1203.

The presumption that non-technical words in a claim have their plain and ordinary English meaning is a strong one. It is only rebutted in situations where "the patentee, acting as his or her own lexicographer, has clearly set forth an explicit definition of the term different from its ordinary meaning" or "if the inventor has disavowed or disclaimed scope of coverage, by using words or expressions of manifest exclusion or restriction, representing a clear disavowal of

claim scope." *Id.* at 1204, *accord, Johnson Worldwide*, 175 F.3d at 989 (modifiers not added otherwise).

Indeed, the importance of non-technical, plain, and ordinary English words in the claims is highlighted by the fact that, of all the intrinsic evidence, the claims are the starting point of claim construction. *Biogen*, 113 F. Supp. 2d at 95-96. For example, to avoid the improper importation of limitations from the specification into the claims, a Court should first seek to "discern the ordinary and customary meanings attributed to the words themselves" before "[c]onsulting the written description and prosecution history." *Texas Digital*, 308 F.3d at 1204.

Of course, if the non-technical, plain, and ordinary English words used by the inventors are clear, the inquiry can stop with the intrinsic evidence. Where claim language is not ambiguous after consideration of the intrinsic evidence, consultation of extrinsic evidence is improper. *Vitronics Corp. v. Conceptroni,c Inc.*, 90 F.3d 1576, 1584 (Fed. Cir. 1996). Extrinsic evidence may never be relied upon to vary or contradict the clear meaning of terms in the claims. *Markman*, 52 F.3d at 981. Extrinsic expert evidence is the most suspect of all: "Once a dispute over claim construction arises, 'experts' should also not be heard to inject a new meaning into terms that is inconsistent with what the inventor set forth in his or her patent and communicated, first to the patent examiner and ultimately to the public. Patents should be interpreted on the basis of their intrinsic record." *Bell & Howell Document Mgmt.Prods. Co. v. Altek Sys*, 132 F.3d 701, 706 (Fed. Cir. 1997).

In addressing the claim construction issues in this case, Ferring has endeavored to adhere to the principles set forth above as enunciated by the Federal Circuit. In particular, with the exception of a single trip to an American English dictionary, Ferring limits itself to intrinsic evidence.

IV. CLAIM CONSTRUCTION PRINCIPLES AS APPLIED TO CLAIMS IN DISPUTE

"In order not to stifle innovation and competition unduly, . . ., '[t]he public generally, and in particular, the patentee's competitors, are entitled to clear and specific notice of what the inventor claims as his invention.'" *Biogen, Inc.*, 113 F. Supp. at 95, citing *Exxon Chem. Patents, Inc. v. Lubrizol Corp.*, 64 F.3d 1553, 1563 (Fed. Cir. 1995).

In each of two groups of patent claim terms at issue in this case, the inventors gave "clear and specific notice" of what was claimed. In the first group, they described methods of using FSH "in the absence of exogenous LH" or "without the presence of exogenous LH." Also in that group of terms, they claimed methods of using FSH with other drugs, and using FSH daily. In the second group of claim terms, they described methods of "suppressing estrogen variability" by the use of particular drugs, what those drugs were, how much of those drugs to give, and particulars about their usage with FSH and LH.

In each instance, the inventors gave "clear and specific notice" what they meant by these elements by using common, everyday language in the claims with ordinary meanings supported by the specifications and file histories.

Fortunately, for the purposes of claim construction, and for the purpose of giving "clear and specific notice," the claims of Serono's patents, for the most part, do not use technical, chemical or medical terms. Instead, the claims – and the disputed terms in them – use clear and common language. Also fortunately, the critical context of those claims as found in the specifications and the file histories is consistent with the ordinary meaning of the words as used in those claims. *Biogen*, 113 F. Supp. 2d at 96 (context of the claim words, as found in specification and prosecution history, is critical).

A. The FSH-Related Claim Terms.

The first group of claim terms include exclusionary language in six claims related to methods of using FSH. In particular, using plain and ordinary English words, they claim methods of "employing FSH as said exogenous gonadotropin in the absence of exogenous LH" ('077 patent claims 1, 2, 8, and 9)[2] or of "employing FSH alone as said exogenous human menopausal gonadotropin without the presence of exogenous LH" ('402 patent claims 1 and 3) (emphasis added).

The abstracts of both patents also use the words "absence of exogenous LH" without any broadening qualification. The specifications of both patents refer to "absence" of LH without any broadening qualification. *See* '077 Patent, col. 3, ll. 12, 19, col. 4, ll 60, 65; '402 Patent, col. 3, ll. 15, 26, col. 6, l. 6 (Staheli Decl., Exs. A and B). Both specifications refer to methods of treating monkeys with "FSH" as a single-named gonadotropin. *See* '077 Patent, col. 3, l. 16 to col. 4, l. 18; '402 Patent, col 3, l. 32 to col. 4, l. 33 (Staheli Decl., Exs. A and B). Both specifications state that the described monkey methods "show that FSH can be administered alone to enhance the natural ovarian cycle." '077 Patent, col. 4, ll. 19-20; '402 Patent, col. 4, ll. 30-33 (Staheli Decl., Exs. A and B).

In the specification of the '077 patent, the inventor of the '077 patent was at pains to point out not only that his method used "only FSH," but that his use of "only FSH" is what made his method novel. In other words, the total and absolute lack of LH was the invention: "It is respectfully submitted that the references cited [the prior art] do not teach or suggest inducing

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[2] Claim 8 of the '077 patent claims a method of "administering FSH as said exogenous gonadotropin in the absence of exogenous LH." '077 Patent, claim 8 (Staheli Decl., Ex. A).

ovulation in a primate or human female by administering exogeneous FSH *in the absence of* exogeneous LH and further do not teach or suggest a method of in vitro fertilization in which such administration of *only* FSH is used cojointly with the administration of a GnRH antagonist in an amount sufficient to suppress endogeneous gonadotropin secretion." '077 Patent Prosecution History, Paper 7, Response to Final Rejection, p. 5 (Staheli Decl., Ex. C) (emphasis added).

The prosecution histories of both patents confirm that the use of FSH and LH together was in the prior art. For example, preamble language to what became independent claims 1 and 8 of the '077 patent specifying that the prior art was methods of using "a combination of FSH and LH" was added to overcome an objection that the language in those claims was unclear as to the prior art. '077 Patent Prosecution History, Papers 6, 7, 14, and 16 (Staheli Decl., Exs. C-F). Also in the '077 prosecution history, to overcome a section 112 enablement objection, and to argue generally against obviousness of the claim of the '077 patent, the inventor argued that "the administration of only FSH in the absence of LH in order to induce ovulation is clearly unobvious." '077 Patent Prosecution History, Amendment Under Rule 115, Paper 16, p. 3 (Staheli Decl., Ex. F). In the '402 prosecution history, the inventors went to lengths to specify what they had invented:

> However, the use of HCG to induce ovulation of follicles which have been matured to a course of treatment which involves administering exogenous FSH in the absence of LH is new. . . . However, those skilled in the art would understand this teaching to refer to the administration of a combination of FSH and LH rather than the administration of FSH alone. . . . Those skilled in the art would not recognize that a reference to the administration of FSH meant the administration of this hormone alone without LH in the absence of an explicit statement in the reference to this effect.

'402 Patent Prosecution History, Paper 3, Amendment Under Rule 115, p. 2. (Staheli Decl., Ex. G).

B. The Estrogen Variability Suppression Claim Terms.

The second group of claim terms relate primarily to methods of suppressing estrogen variability using GnRH-antagonists. Like the first group, the second group of disputed terms also gives "clear and specific" notice by their use of plain and ordinary English words. Claim 13 of the '077 patent, on which 14 and 16 depend, is a method of using GnRH antagonists. The method of '077 patent claim 13 is simply described as being a "method of suppressing estrogen variability in response to gonadotropin treatment." Neither the claim, nor its dependent claims, nor the specification, nor the file history suggest that this method intends any other effect than suppressing "estrogen variability." Indeed, nowhere does the claim, specification, or prosecution history mention another purpose.

Additionally, the claim, the dependent claims, the specification, and the prosecution history refer to the singular and exclusive use of GnRH antagonists to achieve that purpose. There is no mention of using exogenous gonadotropins (such as Bravelle™) to suppress estrogen variability. There is no mention of using exogenous GnRH agonists for this purpose. Quite the opposite. In arguing for what became claims 13, 14, and 16, the inventor was careful to point out his method of using antagonists had a different purpose from methods of infertility treatment using agonists: "Indeed, the purpose of a GnRH antagonist (as distinguished from a GnRH agonist) is to suppress ovulation." '077 Patent Prosecution History, Paper 7, Response to Final Rejection, p. 4. (Staheli Decl., Ex. C).

In both groups of claim terms, the inventors' use of plain and ordinary language to define their inventions, simplifies the Court's construction task. Ferring will discuss below the specific claim construction which it believes is consistent with the intrinsic evidence. For the Court's